



Attorney's Docket No.: 09010-017004 / DIVER 1240-5

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Patrick V. Warren et al. Art Unit : 1652  
Serial No. : 09/481,733 Examiner : Elizabeth Slobodyansky, Ph.D.  
Filed : January 11, 2000  
Title : TRANSAMINASES AND AMINOTRANSFERASES

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

RECEIVED  
SEP 22 2003  
TECH CENTER 1600/2900

DECLARATION UNDER 37 C.F.R. § 1.132

Sir:

1. I, David Weiner, am an expert in the field of molecular biology and enzyme development and was an expert at the time of the invention. I am presently employed as a Principal Scientist at Diversa Corporation, San Diego, CA, assignee of the above-referenced patent application. My resume is attached as documentation of my credentials.

3. I declare that the state of the art at the time of the invention and the level of skill of the person of ordinary skill in the art, e.g., screening enzymes, and nucleic acids encoding enzymes, for transaminase activity, was very high. Using the teaching of the specification, one skilled in the art could have selected routine methods known in the art at the time of the invention to express variants/ modifications of nucleic acids encoding the exemplary enzymes of the invention and screen them for expression of variant/ modified polypeptides having transaminase activity. One skilled in the art could have used routine protocols known in the art at the time of the invention, including those described in the instant specification, to screen for nucleic acids encoding polypeptides having 70% sequence identity to exemplary sequences of the invention, or active fragments thereof, for transaminase activity. One skilled in the art could have used routine protocols known in the art at the time of the invention, including

CERTIFICATE OF MAILING BY FIRST CLASS MAIL

I hereby certify under 37 CFR § 1.8(a) that this correspondence is being deposited with the United States Postal Service as first class mail with sufficient postage on the date indicated below and is addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Date of Deposit

September 12 2003

Signature

Norman Green

Typed or Printed Name of Person Signing Certificate

Applicant : Patrick V. Warren et al.  
Serial N . : 09/481,733  
Filed : January 11, 2000  
Page : 2 of 2

Attorney's Docket No.: 09010-017004 / DIVER 1240-5

those described in the instant specification, to screen for nucleic acids capable of hybridizing under the specific conditions set forth in the specification to exemplary sequences of the invention, or active fragments thereof, for transaminase activity. While the numbers of samples needed to be screened may have been high, the screening procedures were routine and successful results (i.e., finding variant nucleic acids encoding transaminase) predictable. Furthermore, it would not have required any knowledge or guidance as to where modifications needed to be made to create variants/ modified polypeptides having transaminase activity. It would not have required any knowledge or guidance as to which are the specific structural elements, e.g., amino acid residues, that correlate with transaminase activity to create variants/ modifications of the exemplary nucleic acids and test them for the expression of polypeptides having transaminase activity. Accordingly, it would not have taken undue experimentation to make and use the claimed invention, including making and identifying of a genus of nucleic acids encoding transaminases and the enzymes they encode.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Respectfully submitted

Date: 9/11/03



---

David Weiner

# **David Paul Weiner, Ph.D.**

Diversa Corporation  
4955 Directors Place  
San Diego, CA 92121

Phone: (858) 526 5228 Fax: (858) 526-5728

Email: [dweiner@diversa.com](mailto:dweiner@diversa.com)

---

## **Professional Experience**

1997-present      **Principal Scientist, Diversa Corporation.**  

- Discovery and evolution of novel enzymes
- Development of commercially important biocatalytic processes
- Design of efficient routes to important products by combining chemical and biological catalysis
- Director of multidisciplinary team of 15 scientists
- Proven track record in leading partner projects to success with large multinational corporations

1995-1997      **Postdoctoral Research Associate, Departments of Chemistry & Molecular Biology, The Scripps Research Institute. Advisor: Prof. Kim D. Janda.**  

- Designed and generated catalytic antibodies to hydrolyze nucleic acids and polypeptides.

1992-1995      **Postdoctoral Research Associate, Department of Chemistry, Amherst College. Advisor: Prof. David E. Hansen.**  

- Developed strategies for peptidolytic catalytic antibodies.

## **Education**

1988-1992      **Ph.D. University of Leicester, U.K. Chemistry & Biochemistry**  
Thesis title: "Mechanistic studies on DNA gyrase from *E. coli*"  
Thesis advisors: Prof. Paul M. Cullis & Prof. Anthony Maxwell

1985-1988      **B.Sc. (Hons) Biological Chemistry. University of Leicester, U.K.**

1985      **3 A-levels. Brooklands Technical College, U.K.**

1982      **12 O-levels. Kingston Grammar School, U.K.**

## **Professional Societies**

American Chemical Society  
Royal Society of Chemistry  
Faculty of 1000 (invited journal review panel)

## **Other Relevant Experience**

Management skills:      Certificate of Creative Leadership (CCL, San Diego).  
Teamwork skills:      Project leader on numerous projects. Mentor of several employees.  
Language skills:      Fluent Swedish, conversational French.

## Grants Awarded

**Single-cell screen for expression and activity (NIH SBIR phase I: 5/2001 to 11/2001). \$119,840.**

**High throughput discovery of microbial epoxide hydrolases (NIH SBIR phase I: 2/2003 to 8/2003). \$102,500 (Phase II submitted).**

**Directed Biosynthesis of Avermectin Derivatives (NIH SBIR phase I: 5/2003 to 10/2003). \$90,300.**

## Publications

1. Dan E. Robertson, Jennifer A. Chaplin, Grace DeSantis, Mircea Podar, Mark Madden, Ellen Chi, Toby Richardson, Aileen Milan, Mark Miller, David P. Weiner, Kelvin Wong, Jeff McQuaid, Bob Farwell, Lori A. Preston, Xuqui Tan, Martin Keller, Eric Mathur, Patricia L. Kretz, Mark J. Burk, Jay M. Short. **A functional exploration of nitrilase protein sequence space.** (Submitted)
2. DeSantis, Grace; Zhu, Zuolin; Greenberg, William A.; Wong, Kelvin; Chaplin, Jenny; Hanson, Sarah R.; Farwell, Bob; Nicholson, Lawrence W.; Rand, Cynthia L.; Weiner, David P.; Robertson, Dan E.; Burk, Mark J. **An enzyme library approach to biocatalysis: development of nitrilases for enantioselective production of carboxylic acid derivatives.** Journal of the American Chemical Society (2002), 124(31), 9024-9025.
3. Brummer, Oliver; Gao, Changshou; Mao, Shenlan; Weiner, David P.; Janda, Kim D. **Design, synthesis and characterization of panning agents for the selection of metalloantibodies.** Letters in Peptide Science (1999), 6(5-6), 295-302.
4. Brummer, Oliver; Wentworth, Paul, Jr.; Weiner, David P.; Janda, Kim D. **Phosphorodithioates: synthesis and evaluation of new haptens for the generation of antibody acyl transferases.** Tetrahedron Letters (1999), 40(41), 7307-7310.
5. Weiner, David P.; Wiemann, Torsten; Wolfe, Mary M.; Wentworth, Paul, Jr.; Janda, Kim D. **A Pentacoordinate Oxoironium(V) Metallochelate Elicits Antibody Catalysts for Phosphodiester Cleavage.** Journal of the American Chemical Society (1997), 119(17), 4088-4089.
6. Cullis, Paul M.; Maxwell, Anthony; Weiner, David P. **Exploiting Nucleotide Thiophosphates To Probe Mechanistic Aspects of Escherichia coli DNA-Gyrase.** Biochemistry (1997), 36(20), 6059-6068.
7. Smith, Robert M.; Weiner, David P.; Chaturvedi, Nishith C.; Thimblin, Michael D., Jr.; Raymond, Susan J.; Hansen, David E. **Norbornyl dipeptide analogs: mimics of both a transition state and a torsionally distorted ground state.** Bioorganic Chemistry (1995), 23(4), 397-414.
8. Smith, Robert, M.; Ping, Yuan; Weiner, David P.; Dutton, Caryn R.; Hansen, David E. **An approach to sequence-specific antibody proteases.** Applied Biochemistry and Biotechnology (1994), 47(2-3), 329-43.
9. Cullis, Paul M.; Maxwell, Anthony; Weiner, David P. **Energy coupling in DNA gyrase: a thermodynamic limit to the extent of DNA supercoiling.** Biochemistry (1992), 31(40), 9642-6.

10. Weiner, David P. **Expanding the chemistry of nature: catalytic antibodies.** Genetic Engineer and Biotechnologist (1992), 12(2), 9-13.
11. Weiner, David P. **Catalytic antibodies.** Chemistry & Industry (London, United Kingdom) (1991), (10), 347-9.
12. Modha, Jay; Weiner, David P.; Cullis, Paul M.; Rivett, Jennifer. **Effects of ATP analogs on the activity of the Ion proteinase of Escherichia coli.** Biochemical Society Transactions (1990), 18(4), 589.

### **Patents**

1. Greenberg, William; Weiner, David Paul; Adger, Brian; Burk, Mark. **Biocatalytic reduction of nitro groups.** PCT Int. Appl. (2003), 63pp., (WO 0362399 A2 20030731 AN 2003:591312)
2. Barton, Nelson R.; Weiner, David Paul; Greenberg, William; Luu, Samantha; Chang, Kristine; Waters, Elizabeth. **Amidases, nucleic acids encoding them, and methods for making and using them.** PCT Int. Appl. (2003), 204 pp., (WO 0364613 A2 20030807 AN 2003:610600)
3. Desantis, Grace; Chaplin, Jennifer Ann; Chi, Ellen; Milan, Aileen; Short, Jay M.; Weiner, David; Maddes, Mark; Madden, Darcy; Burk, Mark J.; Mathur, Eric. **Environmental microbe nitrilase and gene sequences exhibiting stereoselectivity useful for synthesis of chiral reaction products.** U.S. Pat. Appl. (2003), 105 pp., (US 20030124698 A1 20030703 AN 2003:511968)
4. Weiner, David; Burk, Mark; Hitchman, Tim; Pujol, Catherine; Richardson, Toby; Short, Jay. **Screening, selection, identification and sequences of cytochrome P 450 for use in the production of chiral epoxides.** PCT Int. Appl. (2003), 365 pp. (WO 0352050 A2 20030626 AN 2003:491367)
5. Stege, Justin; Preston, Lori; Weiner, David. **Fusion proteins comprising enzyme, intein, and detectable moiety domains and their use in methods for normalizing enzymic assays.** PCT Int. Appl. (2003), 103 pp. (WO 0350265 A2 20030619 CAN 139:49103 AN 2003:472619)
6. Zhao, Lishan; Mathur, Eric; Weiner, David; Richardson, Toby; Milan, Aileen; Burk, Mark; Han, Bin. **Identification, cloning and sequences of epoxide hydrolases and their use for enantiomeric hydrolysis of epoxides and arene oxides.** PCT Int. Appl. (2003), 400 pp. (WO 0312126 A2 20030213 CAN 138:165742 AN 2003:118029)
7. Weiner, David; Hitchman, Tim; Zhao, Lishan; Burk, Mark. **Methods for the manufacture of pure single enantiomer compounds and for selecting enantioselective enzymes.** PCT Int. Appl. (2003), 122 pp. (WO 0300909 A2 20030103 CAN 138:54642 AN 2003:6148)
8. Madden, Mark; Desantis, Grace; Chaplin, Jennifer Ann; Weiner, David Paul; Milan, Aileen; Chi, Ellen; Short, Jay M.; Burk, Mark. **Bacterial nitrilase and gene sequences exhibiting stereoselectivity useful for synthesis of chiral reaction products.** PCT Int. Appl. (2003), 560 pp. (WO 0300840 A2 20030103 CAN 138:68923 AN 2003:6085)
9. Madden, Mark; Weiner, David Paul; Chaplin, Jennifer Ann. **Producing enantiomerically pure  $\alpha$ -substituted carboxylic acids using stereospecific nitrilases in the presence of**

**Strecker reagents.** PCT Int. Appl. (2001), 87 pp. (WO 0148175 A2 20010705 CAN 135:89140 AN 2001:489604)

### **S 1 ct d Conf r n Pr s ntati ns**

Invited Speaker at the Materials Research Outreach Symposium, January 29-31, 2003, University of Santa Barbara, CA. Talk title: "New opportunities in Biocatalysis".

Keynote speaker at the 2002 DOE Catalysis and Chemical Transformations Workshop, September 20-22, 2002, Chicago, IL. Talk title: "New opportunities in Biocatalysis".

Invited speaker at the 9<sup>th</sup> International Symposium on the Genetics of Industrial Microorganisms, July 1-5, 2002, Gyeongju, Korea. Talk title: "Discovering and Evolving the Best Genes From Nature".

Invited speaker at the Development Center for Biotechnology, July 15, 2002, Taipei, Taiwan. "Discovering and Evolving the Best Genes From Nature".

Invited speaker at the Local Chapter of the American Chemical Society, San Diego, November 13, 2001. "Discovery and Evolution of Novel Biocatalysts".

Speaker at the American Oil Chemists Society, July 20, 2000, San Diego. "Discovery and Evolution of Novel Enzymes"

Biocatalysis Gordon Research Conference, Proctor Academy, Andover, NH, July 1998. "Novel enzymes from biodiversity".

### **Presentations at Companies**

Over 100 presentations on Diversa technologies at multinational companies world-wide.